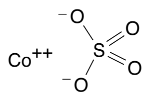
Cobalt Sulfate

CAS No. 10124-43-3

Reasonably anticipated to be a human carcinogen

First listed in the *Eleventh Report on Carcinogens* (2004)



Carcinogenicity

Cobalt sulfate is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to cobalt sulfate by inhalation caused tumors in two rodent species and at two different tissue sites. For inhalation-exposure studies in rodents, the exposure atmospheres were generated as aerosols of cobalt sulfate heptahydrate, containing cobalt ions, sulfate ions, and water, which were partially dried before they entered the exposure chambers. (The hydrated and non-hydrated forms of a solute behave similarly when dissolved in water, both forming a solution of hydrated ions and water.) Inhalation exposure to cobalt sulfate heptahydrate caused lung cancer (alveolar/bronchiolar carcinoma) in mice of both sexes and in female rats, and it increased the combined incidence of benign and malignant lung tumors (alveolar/bronchiolar adenoma and carcinoma) in male rats. It also increased the combined incidence of benign and malignant adrenal-gland tumors (pheochromocytoma) in female rats (NTP 1998).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the carcinogenicity of exposure specifically to cobalt sulfate. However, several studies evaluated the carcinogenicity of cobalt compounds as a class. Most of these studies investigated the effects of occupational exposure to hard metals (cobalt and tungsten carbide) or metallic cobalt (Lasfargues *et al.* 1994, Moulin *et al.* 1998, Wild *et al.* 2000). Although these studies consistently reported an increased risk of lung cancer among workers exposed to cobalt, the workers were also exposed to other agents (e.g., tungsten carbide) and probably were not exposed to soluble cobalt. Thus, these studies are of uncertain relevance for evaluating whether exposure specifically to cobalt sulfate causes cancer. Only one study investigated the effects of exposure to cobalt salts. The initial study reported an increased risk of lung cancer among cobalt production workers, but a follow-up study of the same workers found no increased risk of cancer (Mur *et al.* 1987, Moulin *et al.* 1993). Interpretation of this finding is limited by the small number of exposed workers who developed cancer.

Studies on Mechanisms of Carcinogenesis

Cobalt sulfate did not cause mutations in most bacterial test systems studied, but it did cause genetic damage in many test systems using mammalian cells (NTP 1998). In Syrian hamster embryo cells, cobalt sulfate caused cell transformation (Kerckaert *et al.* 1996) and micronucleus formation (Gibson *et al.* 1997). In mouse fibroblasts, it caused expression of the *p53* tumor-suppressor gene (Duerksen-Hughes *et al.* 1999). In the presence of hydrogen peroxide, cobalt sulfate induced single-strand breaks and apparent intrastrand cross-links in DNA, but not the formation of 8-hydroxy-2′-deoxyguanosine adducts (Lloyd *et al.* 1997, 1998). In human lymphocytes, cobalt sulfate heptahydrate decreased the mitotic index but did not cause micronucleus formation or chromosomal aberrations (Olivero *et al.* 1995).

As a constitutent of vitamin B_{12} (cobalamin), cobalt is absorbed from the gastrointestinal tract, lungs, and skin and is distributed throughout the body. The highest concentrations are found in the liver, kidney, and heart. Cobalt is eliminated primarily in the urine, in two phases: the first phase is rapid and occurs within days, and the second may take several years (Léonard and Lauwerys 1990). The mechanism by which cobalt ions cause cancer has not been determined. It has been suggested that cobalt may replace other essential divalent metal ions (e.g., magnesium, calcium, iron, copper, or zinc), thus altering important cellular functions. Other potential mechanisms include inhibition of DNA repair and interaction with hydrogen peroxide to form reactive oxygen species that can damage DNA (Beyersmann and Hartwig 1992, Lison *et al.* 2001).

Properties

Cobalt sulfate is a cobalt compound that is a reddish to lavender crystalline solid at room temperature. It is soluble in water, sparingly soluble in methanol, and insoluble in ammonia. It is stable at normal temperatures and pressures (Akron 2009). Physical and chemical properties of cobalt sulfate are listed in the following table.

Property	Information
Molecular weight	155.0
Specific gravity	3.71 at 25°C/4°C
Melting point	735°C
Water solubility	383 g/L at 25°C

Source: HSDB 2009.

Use

Cobalt sulfate is used in the electroplating and electrochemical industries; as a drier for lithographic inks, varnishes, paints, and linoleum; in storage batteries; and as a coloring agent in ceramics, enamels, glazes, and porcelain. In addition, cobalt sulfate has been used in animal feeds as a mineral supplement (Budavari *et al.* 1996, Richardson 2003) and on pastures where the forage is cobalt deficient, to provide enough cobalt for ruminants (e.g., cattle, sheep, or goats) to produce vitamin B_{12} (EPA 1999, Washington State 1999). Past uses include addition to beer to improve the stability of the foam (NTP 1998), prevention and treatment of cobalt deficiency in ruminants, and administration to improve blood values (hematocrit, hemoglobin, and erythrocyte levels) in people with forms of anemia not responsive to other treatments (Hillman and Finch 1985, HSDB 2009).

Production

Cobalt sulfate is formed by the interaction of cobalt oxide, hydroxide, or carbonate with sulfuric acid. Production of cobalt sulfate in the United States in 1983 was estimated at 450,000 lb (NTP 1998). No more recent production data were available. Cobalt is no longer mined or refined in the United States, but negligible amounts are produced as by-products of other mining operations (USGS 2003). In 2009, cobalt sulfate was available from 18 U.S. suppliers (ChemSources 2009). In 1986, U.S. imports of cobalt sulfate were 79,700 lb (HSDB 2009). Between 1995 and 2001, annual imports ranged from about 900 metric tons to over 1,600 metric tons (2 million to 3.5 million pounds) (Shedd 2003). No information was found on U.S. exports of cobalt sulfate.

Exposure

No information was found on environmental exposure specifically to cobalt sulfate. The general population may be exposed to cobalt through inhalation of ambient air or ingestion of food or drinking water. Cobalt is an essential trace element in humans, because a cobalt atom is present in each molecule of vitamin B_{12} (Anderson 2000). The 1999 National Health and Nutrition Examination Survey reported the geometric mean cobalt level in the urine of humans to be 0.36 μg/L of urine (95% confidence interval = 0.32 to 0.40) (CDC 2001).

No information was found on occupational exposure specifically to cobalt sulfate. However, more than a million U.S. workers potentially are exposed to cobalt or cobalt compounds (Jensen and Tüchsen 1990). Occupational exposure to cobalt occurs mainly in refining processes, in production of alloys, and in the tungsten carbide hard-metal industry (Kazantzis 1981). In addition, many workers receive limited exposure when using cobalt-containing paint driers. Occupational exposure is primarily dermal or through inhalation of cobalt metal dusts or fumes (NTP 1998, HSDB 2009). Among workers exposed to cobalt, the concentrations of cobalt in blood and urine are closely related to the average levels of cobalt in the air during a workweek (Alexandersson 1988).

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

National Emissions Standards for Hazardous Air Pollutants: Cobalt compounds are listed as hazardous air pollutants.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Cobalt compounds are listed and subject to reporting requirements.

Food and Drug Administration (FDA)

Cobaltous salts are prohibited from use in human food.

All drug products containing cobalt salts (except radioactive forms of cobalt and its salts and cobalamin and its derivatives) have been withdrawn from the market because they were found to be unsafe or not effective, and they may not be compounded.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.02 mg/m^3 for cobalt and inorganic cobalt compounds.

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